Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:SSPTACMB1647

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JAN 12	Match STN Content and Features to Your Information Needs, Quickly and Conveniently
NEWS 3	JAN 25	Annual Reload of MEDLINE database
NEWS 4	FEB 16	STN Express Maintenance Release, Version 8.4.2, Is Now Available for Download
NEWS 5	FEB 16	Derwent World Patents Index (DWPI) Revises Indexing of Author Abstracts
NEWS 6	FEB 16	New FASTA Display Formats Added to USGENE and PCTGEN
NEWS 7	FEB 16	INPADOCDB and INPAFAMDB Enriched with New Content and Features
NEWS 8	FEB 16	INSPEC Adding Its Own IPC codes and Author's E-mail Addresses
NEWS 9	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS 10	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS 11	APR 02	DWPI: New display format ALLSTR available
NEWS 12	APR 02	New Thesaurus Added to Derwent Databases for Smooth Sailing through U.S. Patent Codes
NEWS 13	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS 14	APR 07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS 15	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
NEWS 16	APR 07	MEDLINE Coverage Is Extended Back to 1947
NEWS 17	JUN 16	WPI First View (File WPIFV) will no longer be available after July 30, 2010
NEWS 18	JUN 18	DWPI: New coverage - French Granted Patents
NEWS 19	JUN 18	CAS and FIZ Karlsruhe announce plans for a new STN platform
NEWS 20	JUN 18	IPC codes have been added to the INSPEC backfile (1969-2009)
NEWS 21	JUN 21	Removal of Pre-IPC 8 data fields streamline displays in CA/CAplus, CASREACT,and MARPAT
NEWS 22	JUN 21	Access an additional 1.8 million records exclusively enhanced with 1.9 million CAS Registry Numbers -- EMBASE Classic on STN
NEWS 23	JUN 28	Introducing "CAS Chemistry Research Report": 40 Years of Biofuel Research Reveal China Now Atop U.S. in Patenting and Commercialization of Bioethanol
NEWS 24	JUN 29	Enhanced Batch Search Options in DGENE, USGENE, and PCTGEN

```
 NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
              AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN customer
  agreement.  This agreement limits use to scientific research.  Use
  for software development or design, implementation of commercial
  gateways, or use of CAS and STN data in the building of commercial
  products is prohibited and may result in loss of user privileges
  and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:32:16 ON 29 JUN 2010

=> file medline biosis caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

FILE 'MEDLINE' ENTERED AT 12:32:32 ON 29 JUN 2010

FILE 'BIOSIS' ENTERED AT 12:32:32 ON 29 JUN 2010
Copyright (c) 2010 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 12:32:32 ON 29 JUN 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

=> s (growth(w)hormone or GH)
L1      200481 (GROWTH(W) HORMONE OR GH)

=> s l1 and (circular? or circular(w)permutation)
L2         553 L1 AND (CIRCULAR? OR CIRCULAR(W) PERMUTATION)

=> s l2 and (site(w)2)
L3           7 L2 AND (SITE(W) 2)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           4 DUP REM L3 (3 DUPLICATES REMOVED)

=> s l2 and (GH_CP0?)
L5           1 L2 AND (GH_CP0?)

=> s l2 and (Ile121 or Glu118)
L6           1 L2 AND (ILE121 OR GLU118)

=> dis his

     (FILE 'HOME' ENTERED AT 12:32:16 ON 29 JUN 2010)

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 12:32:32 ON 29 JUN 2010
L1       200481 S (GROWTH(W)HORMONE OR GH)
L2          553 S L1 AND (CIRCULAR? OR CIRCULAR(W)PERMUTATION)
```

```
L3             7 S L2 AND (SITE(W)2)
L4             4 DUP REM L3 (3 DUPLICATES REMOVED)
L5             1 S L2 AND (GH_CP0?)
L6             1 S L2 AND (ILE121 OR GLU118)

=> dis ibib abs l5

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2005:34776  CAPLUS
DOCUMENT NUMBER:          142:127937
TITLE:                    Modified cytokine ligand polypeptides preparation,
                          screening, and uses thereof for treatment
INVENTOR(S):              Sayers, Jon; Artymuik, Peter; Ross, Richard
PATENT ASSIGNEE(S):       Asterion Limited, UK
SOURCE:                   PCT Int. Appl., 45 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005003165         A2    20050113    WO 2004-GB2827          20040628
     WO 2005003165         A3    20050714
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     CA 2568859            A1    20050113    CA 2004-2568859         20040628
     EP 1639002            A2    20060329    EP 2004-743175          20040628
     EP 1639002            B1    20100505
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
     JP 2008504001         T     20080214    JP 2006-518330          20040628
     AT 466880             T     20100515    AT 2004-743175          20040628
     US 20070264234        A1    20071115    US 2007-561831          20070316
PRIORITY APPLN. INFO.:                       GB 2003-15182       A   20030628
                                             WO 2004-GB2827      W   20040628
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The disclosed invention describes modified cytokine ligand polypeptides
     comprising a modified amino acid sequence which is a modification of the
     native cytokine amino acid sequence of said ligand, wherein the native N
     terminal and C terminal amino acid residues of the native polypeptide are
     linked, directly or indirectly, together, characterized in that said
     ligand is provided with alternative N terminal and C terminal amino acid
     residues and further wherein at least one binding domain for said ligand's
     cognate binding partner or receptor complex is disrupted.  The authors
     describe the first embodiment of the growth hormone
     circular permutation GH CP01, with
     the N terminus Ile121 and the C terminus Glu118.  The "old" termini of
     GH were linked by a 6 amino acid linker, formed by joining the
     "old" termini -3 amino acids from the first helix at the N terminus and +3
     residues for the last helix at the C terminus.  E. coli cells were used as
```

the expression system. Also described are alternative approaches to construct circular permutations of GH.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis ibib abs l6

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:34776 CAPLUS

DOCUMENT NUMBER: 142:127937

TITLE: Modified cytokine ligand polypeptides preparation, screening, and uses thereof for treatment

INVENTOR(S): Sayers, Jon; Artymuik, Peter; Ross, Richard

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003165	A2	20050113	WO 2004-GB2827	20040628
WO 2005003165	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2568859	A1	20050113	CA 2004-2568859	20040628
EP 1639002	A2	20060329	EP 2004-743175	20040628
EP 1639002	B1	20100505		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2008504001	T	20080214	JP 2006-518330	20040628
AT 466880	T	20100515	AT 2004-743175	20040628
US 20070264234	A1	20071115	US 2007-561831	20070316
PRIORITY APPLN. INFO.:			GB 2003-15182 A	20030628
			WO 2004-GB2827 W	20040628

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The disclosed invention describes modified cytokine ligand polypeptides comprising a modified amino acid sequence which is a modification of the native cytokine amino acid sequence of said ligand, wherein the native N terminal and C terminal amino acid residues of the native polypeptide are linked, directly or indirectly, together, characterized in that said ligand is provided with alternative N terminal and C terminal amino acid residues and further wherein at least one binding domain for said ligand's cognate binding partner or receptor complex is disrupted. The authors describe the first embodiment of the growth hormone circular permutation GH CP01, with the N terminus Ile121 and the C terminus Glu118. The "old"

termini of GH were linked by a 6 amino acid linker, formed by joining the "old" termini -3 amino acids from the first helix at the N terminus and +3 residues for the last helix at the C terminus. E. coli cells were used as the expression system. Also described are alternative approaches to construct circular permutations of GH.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his

(FILE 'HOME' ENTERED AT 12:32:16 ON 29 JUN 2010)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 12:32:32 ON 29 JUN 2010

L1 200481 S (GROWTH(W)HORMONE OR GH)
L2 553 S L1 AND (CIRCULAR? OR CIRCULAR(W)PERMUTATION)
L3 7 S L2 AND (SITE(W)2)
L4 4 DUP REM L3 (3 DUPLICATES REMOVED)
L5 1 S L2 AND (GH_CP0?)
L6 1 S L2 AND (ILE121 OR GLU118)

=> dis ibib abs l4 1-4

L4 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003280919 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12682073
TITLE: Identification of residues outside the two binding sites that are critical for activation of the lactogenic activity of human growth hormone.
AUTHOR: Duda Karen M; Brooks Charles L
CORPORATE SOURCE: Ohio State Biochemistry Program, Columbus 43221, USA.
SOURCE: The Journal of biological chemistry, (2003 Jun 20) Vol. 278, No. 25, pp. 22734-9. Electronic Publication: 2003-04-07.
Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1A22; PDB-1BP3; PDB-1HGU; PDB-1HWG; PDB-1HWH; PDB-3HHR
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 17 Jun 2003
Last Updated on STN: 22 Aug 2003
Entered Medline: 21 Aug 2003

AB Human growth hormone (hGH) binds lactogenic or somatotrophic receptors, creating active heterotrimeric complexes. Comparison of hGH structures, either free or bound to a single lactogenic or somatotrophic receptor, shows binding is associated with structural changes. Changes in hGH structure are unique when binding either lactogenic or somatotrophic receptors and they influence the spatial arrangement of residues constituting the second receptor-binding site. Using site-directed mutagenesis, we identified a contiguous set of largely hydrophobic residues that forms a motif communicating between the two receptor-binding sites of hGH. The residues are external to the receptor-binding epitopes and were identified when their mutation reduced site 2 function without changing site 1 function. The motif includes Phe44, Leu93, Tyr160, Leu163, and Tyr164, located in two hydrophobic clusters between the receptor-binding sites. Their mutation

to Glu disrupts hydrophobic interactions and reduces lactogenic activity between 4.7- and 85-fold with little effect on somatotrophic activity or spectroscopic properties. These differential effects indicate that loss of lactogenic activity is not a result of global mis-folding. We propose the loss of lactogenic activity results from disruption of specific hydrophobic clusters that disables the site 1 binding-induced structuring of the second receptor-binding site.

L4 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1998298111 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9632658
TITLE: Novel recombinant analogues of bovine placental lactogen. G133K and G133R provide a tool to understand the difference between the action of prolactin and growth hormone receptors.
AUTHOR: Helman D; Staten N R; Grosclaude J; Daniel N; Nespoulous C; Djiane J; Gertler A
CORPORATE SOURCE: Institute of Biochemistry, Food Science and Nutrition, Faculty of Agriculture, The Hebrew University of Jerusalem, Rehovot 76100, Israel.
SOURCE: The Journal of biological chemistry, (1998 Jun 26) Vol. 273, No. 26, pp. 16067-74.
Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 17 Aug 1998
Last Updated on STN: 17 Aug 1998
Entered Medline: 3 Aug 1998

AB Two new analogues of bovine placental lactogen (bPL), bPL(G133K) and bPL(G133R), were expressed in Escherichia coli, refolded, and purified to a native form. Binding experiments, which are likely to represent the binding to site 1 only, to intact FDC-P1 cells transfected with rabbit (rb) growth hormone receptor (GHR) or with human (h) GHR, to Nb2 rat lymphoma cells, or to rabbit mammary gland membranes prolactin receptor (PRLR), revealed only small or no reduction in binding capacity. The complex formation between these analogues and receptor extracellular domains (R-ECD) of various hormones was determined by gel filtration. Wild type bPL yielded 1:2 complex with hGHR-ECD, rat PRLR-ECD, and rbPRLR-ECD, whereas both analogues formed only 1:1 complexes with all R-ECDs tested. Real time kinetics experiments demonstrated that the ability of the analogues to form homodimeric complexes was compromised in both PRLR- and GHR-ECDs. The biological activity transduced through lactogenic receptors in in vitro bioassays in rabbit mammary gland acini culture and in Nb2 cells was almost fully retained, whereas the activity transduced through somatogenic receptors in FDC-P1 cells transfected with rbGHRs or with hGHRs was abolished. Both analogues exhibited antagonistic activity in the latter cells. To explain the discrepancy between the effect of the mutation on the signal transduced by PLR versus GHRs we suggest that: 1) the mutation impairs the ability of site 2 of bPL to form a stable homodimeric complex with both lactogenic and somatogenic receptors by a drastic shortening of the half-life of 2:1 complex; 2) the transient existence of the homodimeric complex is still sufficient to initiate the signal transduced through lactogenic receptors but not through somatogenic receptors; and 3) one possible reason for this difference is that JAK2, which serves as a mediator of both receptors, is already associated with lactogenic receptors prior to hormone

binding-induced receptor dimerization, whereas in somatogenic receptors the JAK2 receptor association occurs subsequently to receptor dimerization.

L4 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1997363737 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9220030
TITLE: Selective modification at the N-terminal region of human growth hormone that shows antagonistic activity.
AUTHOR: Tchelet A; Vogel T; Helman D; Guy R; Neospouolus C; Goffin V; Djiane J; Gertler A
CORPORATE SOURCE: Faculte de Medicine Necker, INSERM, Endocrinologie Moleculaire, Unite 344, Paris, France.
SOURCE: Molecular and cellular endocrinology, (1997 Jun 20) Vol. 130, No. 1-2, pp. 141-52.
Journal code: 7500844. ISSN: 0303-7207. L-ISSN: 0303-7207.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 13 Oct 1997
Last Updated on STN: 13 Oct 1997
Entered Medline: 29 Sep 1997
AB A new analogue of recombinant human growth hormone (hGH), hGH des(1-6,14) was expressed in Escherichia coli, refolded and purified to homogeneity. The mutation decreased the hormone's ability to bind lactogenic and somatogenic receptors through its site 1, and almost completely abolished its ability to bind these receptors through site 2, as evidenced by both binding and gel-filtration experiments. More specifically, the binding to prolactin receptors (PRLRs) from various species or their soluble recombinant extracellular domains (ECDs) was decreased 1.5-4-fold, whereas the binding to hGH receptor (hGHR) was decreased 10-85-fold. These changes caused an almost total loss of hormone agonistic activity in several in vitro bioassays and subsequently, the hGH des(1-6,14) analogue acquired antagonistic properties. This antagonistic activity was dependent upon modification of site 1. In those cases in which the binding was reduced only slightly, e.g. binding to rabbit PRLRs, hGH des(1-6,14) acted as a strong antagonist, whereas in others in which the binding of site 1 was reduced to a higher degree, such as other PRLRs and, in particular, hGHR, the antagonistic activity was correspondingly weaker. Circular dichroism spectra of the analogue suggested that these changes do not result from a decrease in overall alpha-helix content, but rather from minor local structural modifications at the N-terminus.

L4 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 1995096118 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7798264
TITLE: Evidence for a second receptor binding site on human prolactin.
AUTHOR: Goffin V; Struman I; Mainfroid V; Kinet S; Martial J A
CORPORATE SOURCE: Laboratory of Molecular Biology and Genetic Engineering, University of Liege, Sart-Tilman, Belgium.
SOURCE: The Journal of biological chemistry, (1994 Dec 23) Vol. 269, No. 51, pp. 32598-606.
Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 15 Feb 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 24 Jan 1995

AB The existence of a second receptor binding site on human prolactin (hPRL) was investigated by site-directed mutagenesis. First, 12 residues of helices 1 and 3 were mutated to alanine. Since none of the resulting mutants exhibit reduced bioactivity in the Nb2 cell proliferation bioassay, the mutated residues do not appear to be functionally necessary. Next, small residues surrounding the helix 1-helix 3 interface were replaced with Arg and/or Trp, the aim being to sterically hinder the second binding site. Several of these mutants exhibit only weak agonistic properties, supporting our hypothesis that the channel between helices 1 and 3 is involved in a second receptor binding site. We then analyzed the antagonistic and self-antagonistic properties of native hPRL and of several hPRLs analogs altered at binding site 1 or 2. Even at high concentrations (approximately 10 microM), no self-inhibition was observed with native hPRL; site 2 hPRL mutants self-antagonized while site 1 mutants did not. From these data, we propose a model of hPRL-PRL receptor interaction which slightly differs from that proposed earlier for the homologous human growth hormone (hGH) (Fuh, G., Cunningham, B. C., Fukunaga, R., Nagata, S., and Goeddel, D. V., and Well, J. A. (1992) Science 256, 1677-1680). Like hGH, hPRL would bind sequentially to two receptor molecules, first through site 1, then through site 2, but we would expect the two sites of hPRL to display, unlike the two binding sites of hGH, about the same binding affinity, thus preventing self-antagonism at high concentrations.